REMARKS

Claims 1-39 are pending in this application. Claims 6 and 32-39 have been canceled, and claims 1-5, 7-15, 16-21, 27, and 29-31 have been amended. New claims 40-69 have been added. After entry of the amendments herein, claims 1-5 and 7-69 will be pending in the application. No new matter has been added.

Support for the amendments can be found throughout the specification, for examples, at Figure 1 (showing an irradiated plurality of microparticles); page 6, lines 12-13 (irradiated polymeric material); and original claims 4-6 (microparticles). Additional support for amended claims 1 and 16-21 can be found at page 4, lines 19-22 (polymeric materials in the form of an implant, device, suture, or delivery system); page 13, lines 25-27 (significantly less aggregated particles); and Figures 1-4 (showing a substantially non-aggregated plurality of microparticles after irradiation with external cooling). Additional support for the amendments to claims 4 and 5 can be found at page 1, lines 28-30 (microparticles include microspheres and microcapsules). Additional support for the amendments to claims 27 and 29-31 can be found in Figures 1-4 (showing a substantially non-aggregated plurality of microparticles after irradiation with external cooling).

Support for a plurality of substantially non-aggregated microparticles as in new claims 42-67 can be found in Figure 1 (showing a plurality of microparticles); and Figures 2-4 (showing little change in the particle size distribution after irradiation with external cooling) For clarity, Applicants submit herewith enlarged copies of Figures 2 A, B, C and D; 3C "Overlay of Sterilized with Cold Pack and Before sterilization"; and 4D "Overlay of Sterilized with Cold Pack and Before sterilization". Support for an emulsion of microparticles, as in new claims 42-49, 51-58, and 60-67 can be found page 12, line 31. Support for a polymeric implant can be found at page 1, lines 28-30. Additional support for new claims 42-45, 51-54, and 60-63 can be found at Figure 1, particularly batch 3 (showing non-aggregated microparticles after irradiation using external cooling.

Additional support for new claims 46, 55, and 64 can be found at page 14, example 2 (administering microparticles to a patient while suspended in an emulsion). Additional support for new claims 47-49, 56-58, and 65-67 can be found in Figures 2, 4, and 3, respectively (showing particle size distributions of microparticles irradiated using external cooling). Support for new claims 68 and 69 can be found in Figure 1 (plurality of microparticles); Figures 1-4 (showing less aggregation of microparticles sterilized by irradiation using external cooling); and page 13, lines 14-27 (indicating there is less aggregation for batches irradiated below room temperature versus batches irradiated at 25 °C). No new matter had been added.

I. Overview

(A) With regard to the rejection under § 112, second paragraph, it is Applicants' belief that the claims are **definite** because the term "polymeric material" means an implant, a device, a suture, and a delivery system, and does not mean a polymer itself. Polymeric materials are made up of microparticles and the like. Microparticles and the like are made up of polymers.

(B) With regard to the rejection under § 102, it is Applicants' belief that the claims are **novel** because the polymeric materials comprise **substantially non-aggregated microparticles** that are not disclosed by Tice or Rogers.

(C) With regard to the rejection under § 103, it is Applicants' belief that the claims are **not obvious** because the combination of Rogers and Perricone does not teach or suggest an irradiated polymeric material comprised of **substantially non-aggregated microparticles**.

II. Restriction Requirement

The Office Action has required restriction to one of the following groups:

I. Claims 1-31, drawn to a sterile polymeric material and a method of administering said material, classified in class 424, subclass 484, 489.

II. Claims 32-39, drawn to a process of sterilizing polymeric material, classified in class 422, subclass 22.

Applicants note with appreciation the courtesies extended to their representative, Brent Johnson, during a recent telephone call regarding the restriction requirement. During the telephone conversation, Group I was elected orally. Consistent with this election and solely to satisfy 37 CFR 1.143, Applicants hereby elect Group I, claims 1-31, but hereby traverse the restriction requirement on the basis that there is no undue burden to search the claims. In particular, a single search conducted for the irradiative sterilization methods of Group II will substantially overlap with a search for the irradiated polymeric materials of Group I, and any relevant prior references for both Groups would surface. Applicants, therefore, respectfully assert that there is no undue burden on the Office to examine the claims of both Groups.

III. Claims Are Definite

The Office rejects claims 4 and 5 under 35 U.S.C. § 112, second paragraph, stating the claims are indefinite. While acknowledging that the art recognizes using polymeric materials to make microparticles, microcapsules, microspheres, etc., the Action states that the reverse is unclear. That is, the Action requested clarification on how microparticles, microcapsules, microspheres, etc. can make up a polymeric material (Office Action, page 4).

Applicants have amended claim 1, from which claims 4 and 5 depend, to clarify that the term "polymeric material" refers to an implant, a device, a suture, and a delivery system, comprising a plurality of microparticles, rather than the polymer itself. The microspheres and microcapsules of claims 4 and 5 are specific types of microparticles (specification, page 1, lines 28-30). Applicants respectfully assert that one of ordinary

skill in the art understand the scope of the claim as amended. Accordingly, Applicants respectfully request that the rejection under § 112, second paragraph, be withdrawn.

III. Claims Are Novel

The Office rejects Claims 1-12 under 35 U.S.C. § 102, stating that the claims are anticipated by U.S. Patent No. 4,835,139 (hereinafter "the Tice reference") and, in the alternative, by U.S. Patent No. 5,534,261 (hereinafter "the Rogers reference"). Further, claims 13-14 are rejected under 35 U.S.C. § 102 over the Rogers reference alone. The Office states that the present claims are product-by-process claims and that individually the Tice reference and the Rogers reference discloses the same product produced by the sterilization process of the claims.

Applicants respectfully disagree because neither references discloses all of the elements of the amended claims. Applicants have amended claim 1 to recite an irradiated polymeric material comprising a plurality of **substantially non-aggregated** microparticles. Figures 1-4 demonstrate the substantially non-aggregated nature of the microparticles, produced by irradiation using external cooling or at temperatures below 25 °C. By contrast, microparticles irradiated without external cooling or at room temperature are significantly aggregated, as exhibited by the increase in the particle size distribution after irradiation (Figures 1-4).

Neither the Tice nor Rogers reference discloses a plurality of **substantially non-aggregated** microparticles, resulting from irradiation Since the references do not disclose each and every element of the claimed invention, Applicants respectfully submit that neither the Tice nor Rogers reference anticipate claims 1-12, or claims 13-14 in the case of the Rogers reference, and request that the rejections under § 102 be withdrawn.

The Office also rejects claims 16-26 under 35 U.S.C. § 102, stating that the claims are anticipated by the Tice reference or, in the alternative, by the Rogers reference. The Action states that claims 16-26 are methods of administering the product of claims 1-12

(or claims 1-14 in the case of the Rogers reference) (Office Action, pages 6 and 8). Since the product of the present invention is allegedly anticipated by the Tice reference or the Rogers reference, the Action alleges that the method of administering that product is similarly anticipated.

As a preliminary matter, Applicants respectfully assert that claims 22-26 are directed to methods of sterilizing a polymeric material at a temperature below 25 °C and are not methods of administration as alleged by the Action (Office Action, pages 6 and 8). Since neither the Tice reference nor the Rogers reference discloses the use of temperatures below 25 °C for sterilization of polymeric materials, claims 22-26 cannot be anticipated. Applicants, therefore respectfully request that the § 102 rejections based on the Tice reference and the Rogers reference be withdrawn for claims 22-26.

Further, neither the Tice reference nor Rodgers reference anticipate claims 16-21, because neither reference discloses each and every element of the claims. Applicants have amended claims 16-21, to recite a method using the irradiated polymeric materials of claim 2, which comprise a **substantially non-aggregated** plurality of microparticles. As discussed earlier, neither the Tice nor the Rodgers references teaches or suggests an irradiated **substantially non-aggregated** plurality of microparticles. Accordingly, Accordingly, Applicants respectfully request that the § 102 rejections based on the Tice reference and the Rogers reference be withdrawn for claims 16-21.

Additionally, the Office has rejected claims 27-31 under 35 U.S.C. § 102, stating the claims are anticipated by the Tice or Rodgers reference. The Action states that the present claims are product-by-process claims and that individually the Tice reference and the Rogers reference discloses the same product produced by the sterilization process of the claims.

Applicants respectfully disagree because the product of amended claims 27-31 is different than the product of the Tice and Rodgers references. Applicants have amended claims 27-31 to clarify that the compositions comprise a sterilized plurality of

microparticles and therapeutically active agent, wherein the sterilization is accomplished by irradiation with external cooling. The Tice and Rodgers references are silent as to the use of external cooling during sterilization. The temperature range of 4 to 21 °C in the Tice reference refers only to the preferred storage temperature, rather than the temperature used for the sterilization process. The Tice and Rodgers references, therefore, disclose only the sterilization of microparticles at room temperature, without the use of external cooling.

Applicants have surprisingly discovered that the use of external cooling during sterilization of a plurality of microparticles results in a less aggregated product with a narrower particle size distribution as compared with a plurality of microparticles sterilized in the absence of external cooling (see Figures 1-4; and page 13, line 14 to page 14, line 21). Applicants, therefore respectfully assert that the product of the Tice and Rodgers references is an aggregated irradiated plurality of microparticles, similar to that shown in Figures 1-4, for batches of microparticles sterilized by irradiation at room temperature. Accordingly, Applicants respectfully assert that the Tice reference and the Rogers reference do not anticipate claims 27-31 and request that the rejections under § 102 be withdrawn.

IV. The Claims Are Not Obvious

Claim 15, directed to a sterilized polymeric material comprising microspheres, microparticles, or microcapsules and tazarotene, is rejected under 35 U.S.C. § 103 as being allegedly obvious over the Rogers reference in view of U.S. Patent No. 6,365,623 (hereinafter "the Perricone reference"). The Action states that the Rogers reference teaches sterile microparticles made of polylactide-glycolide comprising a retinoid, but does not teach the specific retinoid tazarotene of claim 15 (Office Action, page 9). To overcome this deficiency, the Action combines the Perricone reference, which allegedly discloses that tazarotene is a retinoid (Office Action, page 9). Accordingly, the Action

rejects claim 15 as obvious over a combination of the Rogers reference and the Perricone reference.

In order to establish a **prima facie case of obviousness**, the Office has the burden of showing the following three criteria: 1) a suggestion or motivation to modify or combine the reference teachings; 2) a reasonable expectation of success; and 3) **the teaching of all the claim limitations by the reference(s)**. MPEP § 2143.

Applicants respectfully assert that the Office has not shown that the combination of the Rodgers and Perricone references teaches or suggests the invention of claim 15. Claim 15 depends to claim 1, which Applicants have amended to recite an irradiated polymeric material comprising a plurality of substantially non-aggregated microparticles. Neither the Rodgers nor Perricone reference disclose an irradiated substantially non-aggregated plurality of microparticles as recited by claim 15. Further, both references are silent as to lowered temperature or external cooling during irradiation. Hence, the Rodgers reference, at most, discloses irradiation of microparticles at room temperature. Applicants have shown that irradiation of microparticles at room temperature, without any external cooling, produces microparticles that are significantly aggregated (see Figures 1-4). Hence, at most, the Rodgers reference teaches a significantly aggregated plurality of microparticles, rather than the substantially non-aggregated microparticles of claim 15. Thus, the combination of the Rogers and Perricone reference does not teach or suggest a product having the physical characteristics of the claimed invention (e.g., low level of aggregation of microparticles).

Hence, Applicants respectfully assert that claim 15 is not obvious over the Rogers reference and the Perricone reference. Therefore, Applicants respectfully request that the claim rejection based on § 103 be withdrawn.

Early reconsideration and allowance of all pending claims is respectfully requested. The examiner is requested to contact the undersigned attorney if an interview, telephonic or personal, would facilitate allowance of the claims.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to deposit account 50-1275.

Respectfully submitted,

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Enclosures: Figures 2A-D, 3D and 4D